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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,840	03/13/2001	Gregory R. Mundy	10274-034001	4957

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/04/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,840	MUNDY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *3,6-8 and 10-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/7/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-29 are pending.

2. A clear and obvious typographical error occurred in the restriction wherein claim 7 which reads on alpha4 integrin **ligand** binding agent was improperly included in Groups I and III which are drawn to alpha4 integrin binding agent. Therefore claim 7 is drawn to nonelected inventions.

2. Applicant's election with traverse of Group I, claims 1-2, 4-5, 7 and 9 as they drawn to a method of treating multiple myeloma with alpha4-specific antibody filed on 8/26/02, is acknowledged.

Applicant's traversal is on the grounds that the preambles of Groups I, VI and XI which share the same class and subclass, read on overlapping subject matter and thus should be grouped together. Furthermore, the Examiner has not established that a serious burden would be involved in searching those Groups. This is not found persuasive because the method of treating multiple myeloma, the method of inhibiting bone resorption associated with tumors of bone marrow and the method of treating a subject having a disorder characterized by the presence of osteoclastogenesis differ with respect to endpoints; therefore, each method is patentably distinct and are recognized divergent subject matter. Searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 3, 6-8, 10-29 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-2, 4-5 and 9 are under examination.

5. The oath identifies a wrong filing date (March 13, 1998) for the Provisional application 60/100,182 on which priority is claimed. The Provisional application has the filing date of September 14, 1998 (see attachment).

6. The specification is objected to because the amendment filed on 10/13/01 to the first paragraph of page 1, which claims priority from U.S. Provisional Serial No. 60/100,182, **state** that the Provisional is filed on **March** 12, 1998. The actual filing date for that provisional is **September** 14, 1998. Correction and/or clarifiaction is required.

7. Applicant's IDS, filed 01//07/02 (Paper No. 8), is acknowledged, however, reference AI was crossed out as the entire documents was not found. Applicant is invited to produce such documents.

8. The disclosure is objected to because the " aone" in page 8, line 21 is misspelled. Correction is required.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "antagonist" recited in claim 2 has no antecedent basis in base claim 1. Base claim 1 only recites a composition.

B. Claim 5 is indefinite in the recitation of "fragments thereof" since "antigen binding fragment thereof" has already been recited in base claim 1.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-2, 4, 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Zaanen et al (Br. J. Haematol. 102:783-90, August 1998) in view of Masellis-Smith et al (IDS Ref No. AJ and Lokhorst et al (Blood 84:2269-2277, 1994) and Owens *et al* (1994).

Van Zaanen et al teach a method for treating multiple myeloma comprising administering chimaeric monoclonal anti-IL-6 antibodies (cMab) in multiple myeloma patients, the cMab was given in a dosage of 5-40 mg/d) (see the entire document and the abstract on page 783 in particular).

The Van Zaanen *et al* teaching differs from the claimed invention by not expressly disclosing to employ an antibody anti-alpha4 integrin antibody homolog or antigen binding fragment thereof in claim 1, wherein the composition is an alpha 4 integrin binding agent in claim 2, wherein the anti-alph4 integrin antibody homolog is an antibody homolog that antagonizes the interation of both VLA-4 and alpha4beta 7 with their respective alpha4 ligands, b) and antibody homolog that antagonizes the interaction of VLA-4 with its alpha4 ligand, and c) an antibody homolog that antagonizes the interaction of alpha4beta7 with its alpha4 ligand in claim 4, where in the antibody homolog is selected from the group consisting of a human antibody, a chimeric antibody, a humanized antibody and fragments thereof in claim 5, wherein the antibody homolog is administered at a dose so as to provide from about 0.1 to about 20 mg/Kg body weight in claim 9.

Masellis-Smith et al teach function-blocking monoclonal antibodies such as mAbs against very late antigen 4 that inhibit the CD19+ multiple myelom blood B cell interaction with BM fibroblasts. Furthermore, Masellis-Smith et al teach that the alpha4beta7 ligand is mediated MM blood B cell adhesion (see the entire document and abstract page 930 in particular).

Lokhorst *et a*l teach monoclonal antibodies directed to the α4-integrin (VLA-4) that inhibit binding of purified myeloma cells to long term bone marrow cultures (LTBMC) from patients with multiple myeloma. Furthermore, the antibodies to VLA-4 inhibited the induced IL-6 secreation. Furthermore, Lokhorst *et al* teach that the intimate cell-cell contact is a prerequisite for IL-6 induction and the physical separation of plasma cells and LTBMC by mechanical means such as monoclaonal antibodies to VLA-4 which is involved in the adhesion process, inhibit the induction of IL-6 production by LTBMC. (entire document and abstract page 2269, and page 2276, left column 2nd paragraph in particular).

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a F(ab')$_2$ fragment or a humanized antibody antibodies. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement – dependent cytotoxcity (see the entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody taught by the Van Zaanen *et al* with the antibody that specifically binds

the α4 integrin taught by Masellis-Smith *et al* or Lokhorst *et al*., using human antibody, chimeric antibody, a humanized antibody and fragments thereof as taught by Owens *et al* in a method of treating multiple myeloma (MM).

One of ordinary skill in the art at the time the invention was made would have been motivated to subsiture the anti-IL-6 antibodies with anti-α4 antibodies in a method of treating MM because antibodies against alpha4 integrin inhibit cell-cell contact which is a prerequisite for IL-6 induction as taught by Lokhorst *et al* and because antibodies against alpha4 integrin inhibit the adhesion of alpha4beta7 integrin of B cells from MM patients with its ligand on the bone marrow (BM) fibroblast and hence prevent extravasation into the BM. Further, the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al*.

Claim 9 is included because the determination of the optimal dosage of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. Further, one of ordinary skill in the art would have been motivated to modify and narrow the dosage of the antibodies because all these dosages are overlap with the dosages taught by the Van Zaanen *et al* to treat multiple myeloma.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

13. Claims 1-2, 4-5 and 9 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1-2, 4-5 and 11 of copending Application No. 09/943,659. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
November 4, 2002

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